

Applicants: Cohen and Samuels
U38N: 08/851,628

wherein said [OP/BMP renal therapeutic agent] morphogen induces chondrogenesis in an *in vivo* ectopic bone assay; and wherein said therapeutically effective amount causes a clinically significant improvement in a standard marker of renal function in said mammal.

2. (Three Times Amended) A method of treatment to delay the need for, or reduce the frequency of, chronic dialysis treatments in a mammal in, or at risk of, chronic renal failure comprising

administering to said mammal a therapeutically effective amount of [an OP/BMP renal therapeutic agent] a morphogen, said morphogen comprising an amino acid sequence having at least 70% amino acid sequence homology with the C-terminal seven-cysteine skeleton of human OP-1, amino acids 330-431 of SEQ ID NO:1;

wherein said mammal is not a kidney transplant recipient, and is afflicted with a non-immune, noninflammatory condition [selected from the group consisting of chronic diabetic nephropathy, diabetic glomerulopathy, diabetic renal hypertrophy, hypertensive nephrosclerosis, hypertensive glomerulosclerosis, renal dysplasia, glomerular hypertrophy, tubular hypertrophy, glomerulosclerosis, and tubulointerstitial sclerosis]; wherein said [OP/BMP renal therapeutic agent] morphogen induces chondrogenesis in an *in vivo* ectopic bone assay; and wherein said therapeutically effective amount causes a clinically significant improvement in a standard marker of renal function in said mammal such that said mammal's need for chronic dialysis is delayed or reduced.

3. (Three Times Amended) A method as in claim 1 wherein said [renal therapeutic agent] morphogen comprises a polypeptide comprising at least a C-terminal seven cysteine domain of a protein selected from the group consisting of a pro form, a mature form, and a soluble form of a polypeptide selected from the group consisting of OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP8, [and] BMP9, GDF-5, GDF-6, GDF-7, DPP, Vg1, Vgr-1, 60A, GDF-1, GDF-3, GDF-5, GDF-6, GDF-7, BMP10, BMP11, BMP13, BMP15, UNIVIN, NODAL, SCREW, ADMP, and NEURAL.
4. (Three Times Amended) A method as in claim 3 wherein said [renal therapeutic agent] morphogen comprises a polypeptide consisting of at least a C-terminal seven cysteine

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domain of a protein selected from a group consisting of a pro form, a mature form, and a soluble form of human OP-1.

6. (Twice Amended) A method as in claim 1 wherein said [protein] morphogen has at least 75% homology with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1.
7. (Twice Amended) A method as in claim 1 wherein said [protein] morphogen has at least 80% homology with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1.
8. (Twice Amended) A method as in claim 1 wherein said [protein] morphogen has at least 60% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1.
9. (Twice Amended) A method as in claim 1 wherein said [protein] morphogen has at least 65% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1.
10. (Twice Amended) A method as in claim 1 wherein said [protein] morphogen has at least 70% identity with an amino acid sequence of a C-terminal seven-cysteine domain of human OP-1.
12. (Twice Amended) A method as in claim 1 wherein said [renal therapeutic agent] morphogen is [an osteogenic or bone morphogenic protein] selected from the group consisting of: OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6, BMP8, BMP9, GDF-5, GDF-6, GDF-7, DPP, Vg1, Vgr-1, 60A, GDF-1, GDF-3, GDF-5, GDF-6, GDF-7, BMP10, BMP11, BMP13, BMP15, UNIVIN, NODAL, SCREW, ADMP, and NEURAL.
33. (Amended) A method as in claim 1 wherein said [renal therapeutic agent] morphogen is OP-1.
34. (Amended) A method as in claim 2 wherein said [renal therapeutic agent] morphogen is OP-1.